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13. SUPPLEMENTARY NOTES

14. ABSTRACT - During this third year of the project our efforts have continued to focus on the regulatory aspects of this compleclinical trial. We communicated directly with regulatory experts in the US Army and local Institutional Review Boards (IRBs) athe University of Pittsburgh and the University of Maryland. We have successfully obtained an Investigational Device Exemption from the FDA Center for Devices and Radiological Health Office of Device Evaluation. We subsequently receivedapproval of the proposal from the University of Pittsburgh Institutional Review Board (IRB) as the coordinating center for the trial. We now have approval for the study enrollment, pending community consultation and public disclosure, from the IRBs at the Universities of Pittsburgh and Maryland. The Independent Data Safety and Monitoring Board for this trial has been formeand conducted its first meeting by conference call in December, 2008. We are now working with the Human Research Protection Office to complete the information for the formal Department of the Army review.

15. SUBJECT TERMS
Trauma, hemorrhagic shock, cardiac arrest, cardiopulmonary resuscitation, hypothermia

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Introduction

Cardiopulmonary resuscitation (CPR) can save victims of normovolemic cardiac arrest (CA), e.g., ventricular fibrillation. During exsanguination CA from trauma, however, CPR, even with an emergency department (ED) thoracotomy and open chest CPR, doesn't work. *Emergency Preservation and Resuscitation (EPR)* was developed to rapidly preserve the organism during ischemia, using hypothermia, drugs, and fluids, to "buy time" for transport and resuscitative surgery. The purpose of this study is to test the feasibility of rapidly inducing profound hypothermia ($\leq 10^{o}C$) with an aortic flush in trauma victims that have suffered CA and failed standard resuscitative efforts to enable resuscitative surgery and delayed resuscitation with cardiopulmonary bypass. The primary outcome variable will be survival to hospital discharge with minimal neurologic dysfunction.

Body

Scientific Progress

In December, 2009, we conducted the first meeting of the Data and Safety Monitoring Board. The group approved moving forward with the study. They recommended standardization of the transfusion protocols across sites, elimination of blunt trauma victims, and the use of Seldinger technique for aortic cannulation.

Given the complexity of our planned intervention for trauma patients in cardiac arrest, we need to optimize subject inclusion and exclusion criteria. The literature on such patients is scant, with studies focusing on mortality rates and crude information such as signs of life (pulse, breathing, spontaneous movements) in the field or emergency department and admission cardiac rhythm. To better define this patient population to optimize subject selection, we have initiated a retrospective study at several centers to look at other factors that could be quickly determined during the resuscitation of a trauma patient in the emergency department. This retrospective study should produce publishable data, although so far we have not obtained sufficient data to make any conclusions.

Separately, to better profile patients who die from trauma, we have proposed a study of the hemorrhagic shock database of the Resuscitation Outcomes Consortium, which studies prehospital care in patients with life-threatening injuries. This data should add to our understanding of potential candidates for EPR.

Administrative and Logistic Matters

The first regulatory step for proceeding with this study was to obtain an Investigational Device Exemption (IDE) from the Food and Drug Administration (FDA). Our trial is complicated by the fact that both fluids and equipment are to be used for an application that is not currently approved by the FDA. We have now obtained an investigator-sponsored IDE from the FDA Center for Devices and Radiological Health Office of Device Evaluation.

With the approval of the IDE, we were able to obtain approval for the proposal from the University of Pittsburgh Institutional Review Board (IRB) as both the coordinating center and participating site. Similiarly, the University of Maryland IRB has approved the study. Both IRB approvals are pending completion of the community consultation process. The investigators at the University of Pennsylvania had been working on agreements with their administration and their cardiothoracic surgeons regarding participation in the study. At present, these matters preclude their involvement in the study.

Simultaneously, we have begun the process of human use approval from the USAMRMC. We are working with them to complete all the materials they need for their hierarchy to review the study.

Key Research Accomplishments
The most important accomplishments this past year have been the approvals from the University of Pittsburgh and University of Maryland IRBs for the study. The support and suggestions from the DSMB have also been important

We have begun to collect retrospective data from each site on patients who underwent Emergency Department thoracotomies, presumably potential candidates for resuscitation by EPR. Theses databases are just the beginning of the information that we will need to revise our initial inclusion criteria for the proposed EPR study. We have proposed a similar study within the Resuscitation Outcomes Consortium.

Reportable Outcomes
As this year's efforts have focused on the regulatory issues, there has not been any new research data to report.

Conclusion
Most of the work so far on this project has been focused on the regulatory process. We have an IDE and approval from 2 IRBs. We also have successfully conducted a training session. The next step is to obtain approval from the USAMRMC. In the mean time, we will continue to gather data on current experience with patients who develop a cardiac arrest from trauma and could be candidates for the EPR trial. To this end, we are also exploring the potential for obtaining useful data from the Resuscitation Outcomes Consortium.

References
None